Amendments to the Specification:

-- This application includes a compact disc in duplicate (2 compact discs: Sequence Listing - Copy 1 and Sequence Listing - Copy 2), which are hereby incorporated by reference in their entirety. Each compact disc is identical and contains the following file: US10_089793_feb282002.ST25.TXT.

Disc	DESCRIPTION	SIZE	CREATED	Text File Name	Machine Format and Operating System
Copy 1 Replacement May 13, 2003	Sequuence Listing	1,403416KB	May 13, 2003	US10_089793_feb 282002.ST25.TXT	IBM PC MS-Windows
Copy 2 Replacement May 13, 2003	Sequuence Listing	1,403416KB	May 13, 2003	US10_089793_feb 282002.ST25.TXT	IBM PC MS-Windows

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Please replace the paragraph at page 7, from line 7 through line 9, with the following paragraph:

-- Another embodiment of the invention provides a composition comprising one or more nucleic acids identified in Figure 6A which correspond to the genes disclosed in Figures 14 and 15 ~~15 and Figures 16~~.--

Please delete the following two paragraphs at page 16, from line 13 through line 23 as follows:

~~--Figure 14, is a CD ROM, attached hereto, containing all of the EST sequences identified from the four human cartilage cDNA libraries according to one embodiment of the invention. A subset of sequences in this figure was filed as a CD ROM in U.S. provisional application 60/271,955, filed February 28, 2001 and as a hard copy in U.S. provisional application~~

~~60/275,017, filed March 12, 2001. The names of all of the EST sequences on the CD-ROM are listed in Figures 6B, 6C, 6D and 6E.~~

~~Figure 14A, is a hard copy of a subset of the EST sequences identified in Figure 14 which represents the sequences not filed as a CD ROM in U.S. provisional application 60/271,955, filed February 28, 2001 or as a hard copy in U.S. provisional application 60/275,017, filed March 12, 2001. A CD ROM corresponding to Figure 14A is attached hereto.--~~

Please replace the paragraph at page 16, from line 24 through line 26, with the following paragraph:

--Figure 14 [15], contains a list of genes that have been identified through EST frequency analysis as being differentially expressed between fetal and normal cDNA libraries according to one embodiment of the invention.--

Please replace the paragraph at page 17, from line 1 through line 3, with the following paragraph:

--Figure 15 [16], contains a list of genes that have been identified through EST frequency analysis as being differentially expressed between mild and severe osteoarthritis cDNA libraries according to one embodiment of the invention.--

Please replace the paragraph at page 17, from line 4 through line 8, with the following paragraph:

--Figure 16 [17], is a bar graph showing the level of beta-2 microglobulin (B2M) in synovial fluid from normal individuals and patients with different stages of osteoarthritis according to one embodiment of the invention. Legend: nor=normal individual, mioa=patient with mild osteoarthritis, mooa=patient with moderate osteoarthritis, maoa=patient with marked osteoarthritis, seoa=patient with severe osteoarthritis.--

Please replace the paragraph at page 17, from line 9 through line 11, with the following paragraph:

--Figure 17 [18], is a bar graph showing the level of beta 2 microglobulin (B2M) in medium cultured from cartilage from patients with severe osteoarthritis at varying time periods during culturing according to one embodiment of the invention.

Please replace the paragraph at page 17, from line 12 through line 15, with the following paragraph:

--Figure 18 [19], is a black and white representation of a two-color fluorescent scan according to one embodiment of the invention showing genes preferentially expressed in non-B2M-treated chondrocytes and genes preferentially expressed in B2M-treated chondrocytes. B2M=beta 2 microglobulin.--

Please replace the paragraph at page 29, from line 1 through line 12, with the following paragraph:

--Many human genes are expressed at different levels in cartilage of different developmental (fetal vs. mature) or disease states. In some cases, a gene is not expressed at all in some developmental or disease states, and at high levels in others (see Figure 6, 14 [15] and 15 [16] for examples). According to the invention, differential analysis of chondrocyte gene expression during different stages of cartilage developmental and in different disease states using an EST-based approach has identified genes that play important roles in osteoarthritis pathogenesis and cartilage repair. The advantage of this method is that it provides gene expression information on a larger scale than other methods. The cDNA clones generated by this approach are also useful for functional studies of certain genes. This type of genomic-based approach has provided important novel insights into our understanding of the osteoarthritis disease process and provides for novel diagnostic, prognostic and therapeutic approaches.--

Please replace the paragraph at page 46, from line 5 through line 12, with the following paragraph:

--The EST frequency analysis in Figure 6 (and portions thereof shown in Figures 14 and 15 ~~15 and 16~~) shows the differential gene expression profiles for known genes. Microarrays according to the invention may be used to confirm these profiles and may also be used to show differential expression profiles between different developmental stages and osteoarthritis disease states for novel EST sequences. These novel EST sequences may be further characterized by cluster and alignment analyses to determine how many unique genes are represented by the novel EST sequences. The novel unique genes identified may provide a basis for identifying key markers in osteoarthritis disease progression and treatment.--

Please replace the paragraph at page 78, from line 2 through line 8, with the following paragraph:

-- Genes that are differentially expressed as defined herein between normal, mild, severe and fetal cartilage were identified through relative EST frequency analysis (see Figure 6). Of the 5,807 known unique genes identified in Figure 6, 405 genes were found to be expressed in all four tissue types. Examples of possible subanalysis are shown in Figures 14 and 15 ~~15 and 16~~. Some of these genes with particularly marked differential expression are shown in Figure 4. The relative frequency of ESTs representing collagens (Figures 2 and 3) and selected extracellular matrix proteins (see Figure 1) were also analyzed.--

Please replace the paragraph at page 82, from line 14 through line 25, with the following paragraph:

-- Analysis of a microarray comprising some of the sequences in the sequence listing ~~Figure 14~~, resulted in 36 candidate upregulated genes in the mild OA library that showed a greater than 2-fold median ratio and 47 candidate downregulated genes that showed a less than 0.2-fold median ratio (Figures 9 and 10, respectively,). A total of 38 candidate upregulated genes were also identified in the severe OA library that showed a greater than 2-fold median ratio and 51 candidate downregulated genes that showed a less than 0.2-fold median ratio (Figures 11 and 12, respectively,). According to this embodiment, the microarray was hybridized with a target nucleic acid sample derived from an individual diagnosed with mild osteoarthritis and a target nucleic acid sample derived from an individual diagnosed with severe osteoarthritis. As would be clear to a person skilled in the art, similar analysis can be performed for any of the sequences identified in Figure 13, or the sequences identified in Figure 6A which correspond to the genes disclosed in Figure 6 using the methods disclosed herein.--

Please replace the paragraph at page 88, from line 12 through line 15, with the following paragraph:

--The average B2M levels detected in normal (nor), mild (mioa), moderate (mooa), marked (maoa) and severe OA (seoa) synovial fluid are shown in Figure 16 [17]. B2M in osteoarthritis synovial fluid is significantly higher than that in normal. However, no significant difference was found in B2M levels among different osteoarthritis stages.

Please replace the paragraph at page 88, from line 16 through line 20, with the following paragraph:

--To assess if chondrocytes contribute B2M secretion, medium from cultured severe OA cartilage was collected and tested for B2M. Figure 17 [18] shows the release of B2M is detectable after 24 hour culture and continues to increase during the 72 hour study period. At 72 hours, the accumulation of B2M was about 2.1 ug/g cartilage. Similar results were obtained across three experimental runs, each using cartilage from a different donor.--

Please replace the paragraph at page 88, from line 21 through line 28, with the following paragraph:

--Genes regulated by B2M were detected through microarray technology as described above. Figure 18 [19] shows a black and white representation of a two-color fluorescent scan. Cy3 labeling (which would appear as green spots) correspond to genes preferentially expressed in non-B2M treated chondrocytes, while Cy5 labeling (which would appear as reddish spots) represent genes preferentially expressed in B2M treated chondrocytes. Genes expressed at approximately equal levels would appear as yellow spots. The identity of genes was determined by the location of nucleic acid members on the array. Some of the genes that were up or down-regulated at least two-fold by B2M are listed in Table 8.--